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Progression and risk factors of pododermatitis in part-time group housed rabbit does in Switzerland

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ABSTRACT

In rabbits (*Oryctolagus cuniculus L.)*, pododermatitis is a chronic multifactorial skin disease that appears mainly on the plantar surface of the hind legs. This presumably progressive disease can cause pain leading to poor welfare, yet the progression of this disease has not been thoroughly assessed on the level of individual animals. The aim of this longitudinal study thus was to investigate the possible risk factors and the progression of pododermatitis in group housed breeding does in Switzerland on litter and plastic slats.

Three commercial rabbit farms with part-time group housing on litter and plastic slats were visited every four weeks throughout one year. During every visit, the same 201 adult female breeding rabbits (67 does per farm) were evaluated for the presence and severity of pododermatitis. Additionally, the does' age, parity, body weight, reproductive state, hybrid, claw length, cleanliness and moisture of the paws and the temperature and humidity inside the barns were recorded as potential risk factors. The risk factors were analysed through general linear models and additive Bayesian network (ABN) modelling using a directed acyclic graph (DAG) for visualising associations between potential risk factors. The progression of pododermatitis was analysed with a transition matrix.

Relative humidity inside the barns, body weight, number of kindlings, age, and claw length were the most important risk factors, all being positively associated with pododermatitis. In contrast to expectations, the cleanliness of the left hind paw was negatively associated with the occurrence of pododermatitis, but the effect was small. In young does, the severity of pododermatitis quickly increased and in some rabbits proceeded to ulcerated spots. It was shown that 60.00%, 14.17% and 3.33% of ulcerated lesions recovered to a state without ulceration within 4, 8 or > 12 weeks, respectively.

1. Introduction

Pododermatitis, also called sore hocks or foot pad lesions, is a chronic granulomatous, ulcerative dermatitis of multifactorial aetiology. In rabbits, it mainly appears on the plantar metatarsal and, occasionally, volar metacarpal and phalangeal surfaces of the feet (Hess and Tater, 2012). The disease starts off with hairless regions with thickened skin that eventually ulcerate and start bleeding. Some of the suggested risk factors for pododermatitis are directly linked to the animals themselves, like breed, age, body weight or claw length (Rommers and Meijerhof, 1996). Other risk factors are related to the rabbits' environment, such as high temperatures, humidity (Lebas et al., 1986 in Rommers and Meijerhof, 1996), wire floors or wet and dirty litter (EFSA, 2005; Harcourt-Brown, 2002).

Pododermatitis is a common condition in commercial rabbit production (Buijs et al., 2014; EFSA, 2005; Olivas et al., 2013). The final stages are thought to be painful (Drescher and Schlender-Böbbis, 1996; EFSA, 2005; Harcourt-Brown, 2002) and severe wounds due to pododermatitis can be a reason for the premature slaughter of a doe (EFSA, 2005; Olivas et al., 2013). Therefore, pododermatitis is a serious threat to the welfare of affected animals. In Europe, breeding does on commercial farms are commonly single-housed in cage systems with wire

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mesh floors (Buijs et al., 2014; EFSA, 2005), and most previous studies on pododermatitis focused on this housing system. In Switzerland, group housing of breeding does in pens with litter and plastic slats offers an alternative that better fulfils the rabbits behavioural needs (Andrist et al., 2013). It provides more space allowing the animals to exhibit a wider behavioural repertoire (Mugnai et al., 2009) and gives them the opportunity for positive social contacts (Seaman et al., 2008). According to Szendrö and McNitt (2012), the most important disadvantages of group housing systems compared to single housing systems are lower reproductive performance, higher production costs, and potentially harmful agonistic interactions.

The aim of this longitudinal study was to describe the course of pododermatitis lesions over time, and to assess which factors promote the progression of pododermatitis in Swiss group housing systems. To our knowledge, this is the first study where the same does were scored repeatedly over one year, which allowed us to track the progression of pododermatitis on an individual level. It complements the cross-sectional study by Ruchti et al. (2018) that reported high variability in the prevalence of severe pododermatitis in does on litter and plastic slats (4%–49% of the does per farm were affected by painful pododermatitis), but failed to identify risk factors for pododermatitis accounting for the majority of this variability during the instantaneous data collection.

2. Material and methods

2.1. Ethical statement

This study was conducted in compliance with the Swiss regulations on animal experimentation and was formally approved by the Veterinary Office of the Canton of Bern (License no. BE 8/14 and BE 123/16).

2.2. Study design

We conducted a longitudinal study on three commercial Swiss rabbit farms with group housing of breeding does that belong to the Kani-Swiss GmbH (www.schweizerkaninchen.ch, accessed 16/10/2017) with the animal friendly housing label BTS (https://www.kontrolldienst-sts.ch/html/index.php/de/coop-bts-kaninchen, accessed 23/10/2017). The farms were visited every four weeks for two days from July 20, 2016 until June 30, 2017 (13 visits per farm). Initially, 67 adult does (after their 1st insemination) were randomly chosen on each farm (201 rabbits in total) that were scored for pododermatitis during every visit. Group sample size calculations corrected for clustering of rabbits within pens within stables with 200 animals predicted 80% power to detect an odds ratio of 2.0 in a design with 9 repeated measurements. Due to the loss of does (death or culling), 46, 51 and 47 animals on farms 1, 2, and 3, respectively, had to be replaced by new does. In addition to the pododermatitis scoring, various potential risk factors were recorded during every visit.

2.3. Animals and housing

Two different hybrids were used. Farm 1 used Hyla (http://www.eurolap.fr/en/hyla-ng.html, accessed 10/04/2018) and farms 2 and 3 used Hycole (http://www.hycole.com/en/, accessed 23/10/2017) rabbits. In total 113 (97 Hyla + 1 Hycole + 15 F1 = Hyla x Hycole or HYLAMAX; http://www.eurolap.fr/en/hylamax.html, accessed 10/04/2018), 118 (111 Hycole + 7 F1 = Hycole x Hyla or ZIKA; http://www.zika-kaninchen.de/, accessed 23/10/2017) and 114 (114 Hycole) does were scored on farms 1, 2 and 3, respectively. The housing system is explained in more detail in Ruchti et al. (2018).

2.4. Data collection

2.4.1. Selection of does and pens

On each farm, 67 adult does were initially caught in a stratified manner controlling for the location of the animal within the pen and choosing at least one doe per pen, excluding pens with non-pregnant does. The does were kept inside one barn on farms 1 and 3 whereas farm 2 had two different barns where 34 and 33 does were selected in barns 1 and 2, respectively. To enable the identification of the animals over time, only does wearing ear tags were scored. Rabbits that could not be identified anymore (loss of ear tag), died or were culled during data collection were randomly replaced by other does of the same farm. Does for replacement were randomly chosen (regardless of age) out of the pens where no or the least number of selected does were left, again excluding the pens with non-pregnant does. Animals in a moribund health state were not selected for scoring and reported to the breeder. After data collection, the does were returned into their groups and remained on the farms.

2.4.2. Pododermatitis- and risk factor-scoring on animal level

Two different localisations, "heel" and "middle" (for details see Ruchti et al. (2018)), were scored for pododermatitis by manual palpation (without gloves) on the plantar surface of every hind paw by one person (SR). A tagged visual-analogue scale following the scores by Drescher and Schlender-Böbbis (1996) was used whereas score 0 represented a healthy paw with normal amount of fur; score 1 reddened skin with hypotrichosis or alopecia; score 2 low-grade hyperkeratosis with hypotrichosis or alopecia; score 3 hyperkeratosis with alopecia and scaling; score 4 hyperkeratosis with alopecia, scabs from clear wound secretion and beginning ulceration; score 5 hyperkeratosis with alopecia, scabs from bloody wound secretion and ulceration and score 6 hyperkeratosis with alopecia, crusts from bloody wound secretion, deep ulceration and degeneration of the surrounding tissue (for details see Ruchti et al. (2018)). To ensure equal quality in terms of lighting conditions between different farms, a headlamp was used to score the paws.

In addition to pododermatitis, the cleanliness (binomial variable) and moisture (multinomial variable) of the fur on the plantar surface of both hind paws, as well as the claw-length (binomial variable), body weight in kg rounded to the second decimal place, hybrid (multinomial variable), age in months, number of kindlings and the reproductive state (multinomial variable) were noted for every doe. See Table 1 for the levels of binomial and multinomial variables.

2.4.3. Risk-factor measurements inside the barn

During the whole year of data collection, the temperature and relative humidity inside the barns were measured every 30 min using a HOBO® data logger U10-003 (Onset Computer Corp., Bourne, MA 02532). For the analysis, the mean temperature and mean relative humidity of the four weeks between the visits were used for every barn. The only exception was the first visit when only the average of the first day of data collection was used. As farm 2 had two barns, two different data loggers were used to obtain one value per barn.

2.5. Statistical analysis

The data processing was performed using Excel 2010. The exploratory data analysis and the risk factor analysis were performed in R (version 3.2.5, R Development Core Team, 2016) using mainly the R package abn (Kratzer et al., 2017). The data were stored and exchanged using a web-based hosting service for version control using git as well as all the analysis related documents.

2.5.1. Data management

A total of 26 variables were recorded at different grouping levels. The data were imported through a scripted procedure using R to

Table 1
Descriptive statistics (counts or median and range) of the variables that were used for the risk factor analysis including 13 observations per farm on barn-level and 871 observations per farm on animal-level (multiple observations per barn and per animal), NA = missing values. For categorical variables counts are given, for continuous variables the median and the range are given.

Variable	Farm 1	Farm 2	Farm 3
Barn-level			
RelativeHumidity[1]	66.95 [55.43 – 76.80]	67.21 [55.47 – 78.22]	62.92 [57.13 – 67.09]
Temperature[2]	17.09 [11.92 – 26.00]	14.61 [9.08 – 26.10]	18.05 [10.75 – 23.68]
Animal-level			
PDmiddle[3]	3.95 [0.00 – 8.05] (2 NA)	3.85 [0.00 – 7.95] (4 NA)	3.85 [0.00 – 6.95] (4 NA)
PDheel[4]	3.80 [2.20 – 5.85] (2 NA)	3.80 [2.00 – 6.35] (7 NA)	3.90 [2.30 – 5.65] (4 NA)
MoistHR[5]			
- Dry	479	585	546
- Moist	299	203	252
- Wet	93	83	73
MoistHL[6]			
- Dry	444	555	505
- Moist	319	235	288
- Wet	106	77	75
- NA	2	4	3
Hybrid			
- F1	68	48	0
- Hycole	5	823	871
- Hyla	798	0	0
Reproductive State			
- Not pregnant	122	67	78
- Only lactating	235	246	192
- Early pregnancy/ lactating	167	179	245
- Middle pregnancy/ lactating	166	254	149
- Late pregnancy	181	125	207
No Kindlings	7 [0 – 21]	7 [1 – 24]	6 [0 – 23]
Age	16 [3 – 39]	17 [4 – 43]	14 [5 – 41]
Weight	5.14 [2.73 – 6.93]	5.21 [3.07 – 6.87]	5.00 [2.86 – 6.94] (1 NA)
CleanHR[7]			
- Clean	664	700	683
- Dirty	207	171	188
CleanHL[8]			
- Clean	668	714	673
- Dirty	200	152	195
- NA	3	5	3
Claw length			
- Normal	532	398	687
- Too long	335	466	181
- NA	4	7	3

[1] Mean relative humidity inside the barn in %.
[2] Mean temperature inside the barn in °C.
[3] Mean of the two pododermatitis scores from the middle positions per animal.
[4] Mean of the two pododermatitis scores from the heel positions per animal.
[5] Moisture of the fur on the plantar surface of the right hind leg.
[6] Moisture of the fur on the plantar surface of the left hind leg.
[7] Cleanliness of the fur on the plantar surface of the right hind leg.
[8] Cleanliness of the fur on the plantar surface of the left hind leg.

aggregate them in a database. To increase the quality of the database multiple data cleansing tests were performed: data-type constraints tests, data range tests and regular expression patterns checks. Then an exploratory data analysis was performed to check for unexpected pattern in the data.

2.5.2. Statistical approach

A multivariate data driven modelling approach was used to analyse this dataset in order to understand the latent structure of the data. Additive Bayesian network (ABN) modelling is a machine learning approach that is well suited to sort out directly from indirectly related variables. A new scoring procedure is used to identify the maximum a posteriori Bayesian network (Kratzer and Furrer, 2018). The final model is represented by a directed acyclic graph (DAG) where the nodes of the network are the random variables and the edges are the relationships between them. The network scores and the relationships are computed using a generalized linear modelling framework and the distribution depends on the index node (Lewis and Ward, 2013).

The actual R implementation of ABN suffers of two main limitations. The continuous, binomial and Poisson distributions are implemented but not the multinomial distribution. When a multinomial random variable should be integrated into the modelling process it must be split into binomial random variables. Although being a popular workaround (Lewis and Ward, 2013) this is not entirely satisfactory from a modelling point of view as the split variables lose their former natural links. Another limitation of this approach is the numerical instability link to the sparsity in the data. This problem is common in classical binomial regression but it becomes astoundingly common in an ABN analysis as all possible combinations are tested. This is called the (quasi) data separation problem. Those two limitations motivate the implementation of the ABN methodology using a frequentist approach (Kratzer and Furrer, 2018). The scores used to identify the Bayesian network are not Bayesian based but are information theoretic based. In this project the Bayesian Information Criteria (BIC) was used.

The ABN procedure is computationally highly sensitive to the allowed number of parents per node. An ABN search is performed in sequentially increasing the number of parents. Once the maximum a posteriori score does not increase anymore, the index number of parents is set as the required complexity of the network. Then a non-parametric bootstrap procedure with replacement is applied to avoid over fitting. 10,000 bootstrap samples with replacement were simulated. The arcs supported by at most 50% of the bootstrap samples were kept in the final pruned network.

2.5.3. Exploratory data analysis

As the does were kept in similar housing conditions and because the distribution of the variables looked similar across the farms, the three farms were treated as comparable and no clustering adjustment was included into the ABN procedure.

2.5.4. Risk factor analysis

To perform the risk factor analysis of pododermatitis, a subset of 14 relevant variables was chosen based on literature and expert opinion. Out of it, seven, three and four variables had a continuous, binomial and multinomial distribution, respectively. In the model, the mean of the two pododermatitis scores from the heel and the mean of the two pododermatitis scores from the middle location of the hind legs were used for every rabbit. The risk factor analysis was done in R using the abn package (Kratzer et al., 2017; Kratzer and Furrer, 2018) for the ABN analysis. It was performed without considering the longitudinal component of the data, which was done with a transitional model. In this context a transitional model is a matrix giving the probability, computed using observed counts, of the evolution of the staging of the pododermatitis.

Additionally, a general linear model with repeated measures was performed using Proc Glimmix (SAS® 9.4) with REML and an autoregressive (AR(1)) covariance structure with farm as a fixed and the does nested in farm as a random effect. Two models were run. The first model included the same factors that were related to pododermatitis in the DAG of the risk factor analysis and the second model additionally included the reproductive state of the doe. In both cases all two-way interactions were included initially but subsequently removed unless the P-value was below 0.2.

To investigate the relationship between culling/dying during the study and pododermatitis a generalized linear model was performed with age as the covariate using Proc Glimmix (SAS® 9.4). Visualization of the residuals was used to evaluate the fit of the model.

2.5.5. Longitudinal component of the pododermatitis

Over one year, the same does were scored every four weeks totalling 13 times. This allowed us to study the progression of the pododermatitis score trajectorially per animal. To study this longitudinal component of the data, a transition matrix for the mean of the two pododermatitis scores from the middle location of the hind legs was computed using the individual score trajectories. The matrix was computed using normalised count transition and was normalized by column, which means that the numbers represent the probability to go from the current score to the row-wise score.

3. Results

3.1. Repeatability of the pododermatitis-scoring

The repeatability of the pododermatitis score assessed prior to the actual data collection was good (see Ruchti et al., 2018). As the pododermatitis score of the heel was less variable as compared to the middle area of the paw, the focus of the analysis and interpretation was placed on the pododermatitis score from the middle location of the hind paws.

3.2. Risk factors

The mean age of the does increased from 14.02 months (range: 4–35 months) during the first visit to 18.69 months (range: 5–40 months) at the last visit. Similarly, the mean number of kindlings increased from 5.81 (range: 0–18) during the first visit to 8.62 (range: 1–23) at the last visit. Overall, the does on farms number 1 and 2 were slightly older, thus had more kindlings and were heavier than the rabbits on farm number 3 (Table 1). The descriptive statistics of all the variables that were included in the risk factor analysis are shown in Table 1 for every farm.

Fig. 1 shows the DAG from the ABN analysis; Table 2 shows the corresponding regression coefficients of the arcs. The cleanliness of the left hind leg was negatively associated with the pododermatitis score, our variable of interest, whereas the relative humidity, body weight, and number of kindlings were positively associated with pododermatitis. The cleanliness and moisture of the right and left hind legs were strongly correlated with each other. Similarly, the temperature was strongly negatively correlated with the relative humidity and the age of the animals which itself had a strong positive correlation to the body weight and the claw length. Especially during the winter months (sampling points 6–8) the relative humidity was much lower on farm 3 than on farms 1 and 2 (Fig. 2).

The general linear model confirmed the results of the DAG. Farm was not a significant factor for pododermatitis but body weight, number of kindlings, and the cleanliness of the left hind leg were (see supplementary data S.1). As in the DAG the association between body weight and pododermatitis was positive (0.44; CI95% (0.22, 0.66)), the association between relative humidity and pododermatitis was slightly negative (-0.02; CI95% (-0.04, 0)) and between number of kindlings and pododermatitis positive (0.28; CI95% (0.18, 0.38)). The relationship between body weight and relative humidity was different for different farms (significant interactions). In the model including state of reproduction its relationship with pododermatitis differed for different farms and number of kindlings. Furthermore, there were interactions between body weight and farm and relative humidity and farm.

3.3. Development of pododermatitis over time

Across all visits (2613 observations of the mean of the two pododermatitis scores, multiple observations per doe), the following proportions were obtained for does with pododermatitis scores 0-6: score 0: 2.22%, 1: 0.92%, 2: 14.96%, 3: 71.57%, 4: 8.27%, 5: 1.68% and 6: 0.00%. The scores 4–6 were assumed to be painful for the animals. Fig. 3 shows the distribution of the pododermatitis score over time for every farm.

From the does that were first scored at the age of 3–5 months (n = 34, nulli- and primiparous does, multiple observations per doe), score 0 was recorded for 20.59% of the does, score 1 for 2.94%, score 2 for 23.53% and score 3 for 41.18%. When they were first scored, 2.94% already had score 5 and 8.82% could not be scored due to matted fur on the plantar surface of their feet that could not be removed without washing or shaving. The matted fur was a transient state, so the affected does could be scored during following visits. Table 3 shows the transition matrix of the mean of the two pododermatitis scores per animal with the probabilities to go from the current score to the score at the next visit. Score 3 was the most frequent score and 81% of the does with this score remained at a score 3 at the next palpation. The most frequent transitions were from score 2 to score 3 and from score 3 to score 2.

Out of the 345 does that were scored during this study, 136 or

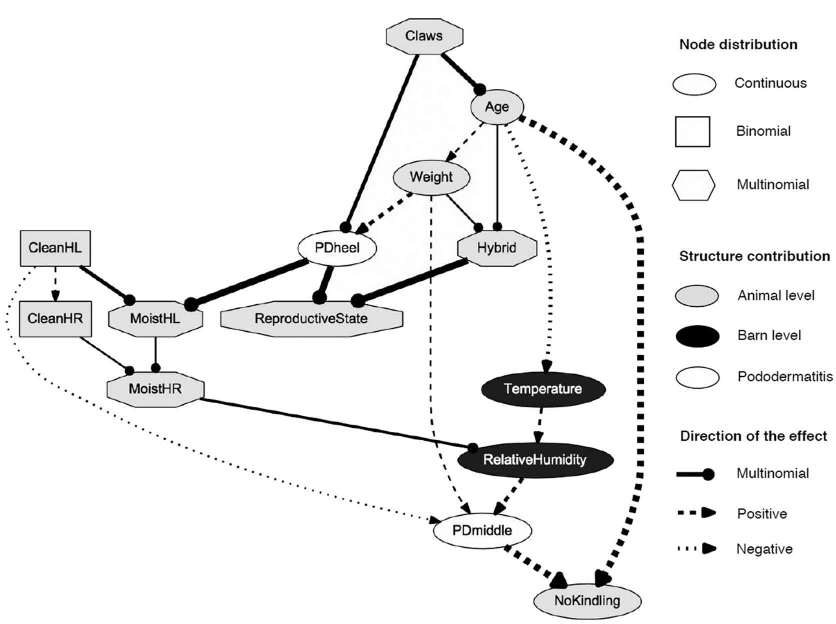

Fig. 1. Directed acyclic graph (DAG) obtained after 10′000 non-parametric bootstrapping runs, n = 2565. The thickness of the arcs is proportional to the bootstrapped frequency, which is assumed to be a proxy for the strength of the support of the arc by the data. The direction of the arcs shows associations, not causations. See Table 1 for the explanation of abbreviations.

Table 2
Regression coefficients of the arcs displayed in the directed acyclic graph (DAG) in Fig. 1. The variables are arranged in descending order by the number of parents. The rows are the regression coefficients of the parents of the index node. The regression coefficient between a Gaussian node and a Gaussian covariate measures the strength of the linear relationship between those two variables. The value always lies between +1 and -1. Example: If the relative humidity increases by 1%, PDmiddle is expected to increase by 0.0003. The regression coefficients for binomial (emphasised in bold) and multinomial (emphasised in italic) nodes are presented as an odds ratio. The values represent the strength of association between nodes. For the binomial variables, the state "normal" was used as baseline for "Claws" and the state "clean" was used as baseline for the variables "CleanHR" and "CleanHL". Example: Compared to animals with clean paws (CleanHL: "clean" = baseline), rabbits with dirty paws are expected to have a -0.2 lower score of PDmiddle. See Table 1 for the explanation of abbreviations.

Variables	PD middle	PD heel	Moist HR Dry	Moist HR Moist	Moist HR Wet	Moist HL Dry	Moist HL Moist	Moist HL Wet	Hybri d F1	Hybri d Hycole	Hybri d Hyla	Repro-ductive State	NoKind-lings	Rela-tive Humi-dity	Tem-pera-ture	Age	Weight	Clean HR	Clean HL	Claws
PDmiddle	–													0.0003			0.248		−0.207	
PDheel		–															0.050			−0.027
MoistHR			–	–	–															
Dry	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Moist			–	–	–	*2.054*	*−5.081*	*−19.963*										*0.478*		
Wet			–	–	–	*−4.174*	*0.893*	*2.863*										*0.286*		
MoistHL			–	–	–	–	–	–												
Dry	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Moist		*1.844*				–	–	–											*1.558*	
Wet		*−0,696*				–	–	–											*−0.022*	
Hybrid									–	–	–									
F1	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Hycole									–	–	–					*0.061*	*0.081*			
Hyla									–	–	–					*−2.958*	*−2.736*			
ReproductiveState												–								
Not pregnant/ lactating		*0.996*							*−2.149*	*−7.199*	*0.064*	–								
Only lactating		*−0.031*							*0.169*	*0.465*	*−0.030*	–								
Early pregnancy/ lactating	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Middle pregnancy/ lactating		*0.486*							*−3.229*	*−7.469*	*−0.155*	–								
Late pregnancy		*1.284*							*−5.063*	*−4.215*	*0.303*	–								
NoKindlings	0.004												–			0.577				
RelativeHumidity			73.659	73.689	73.710									–	−0.458					
Temperature															–	−0.010				
Age																–				5.088
Weight																0.011	–			
CleanHR																		–	**13.734**	
CleanHL																			–	
Claws																				–

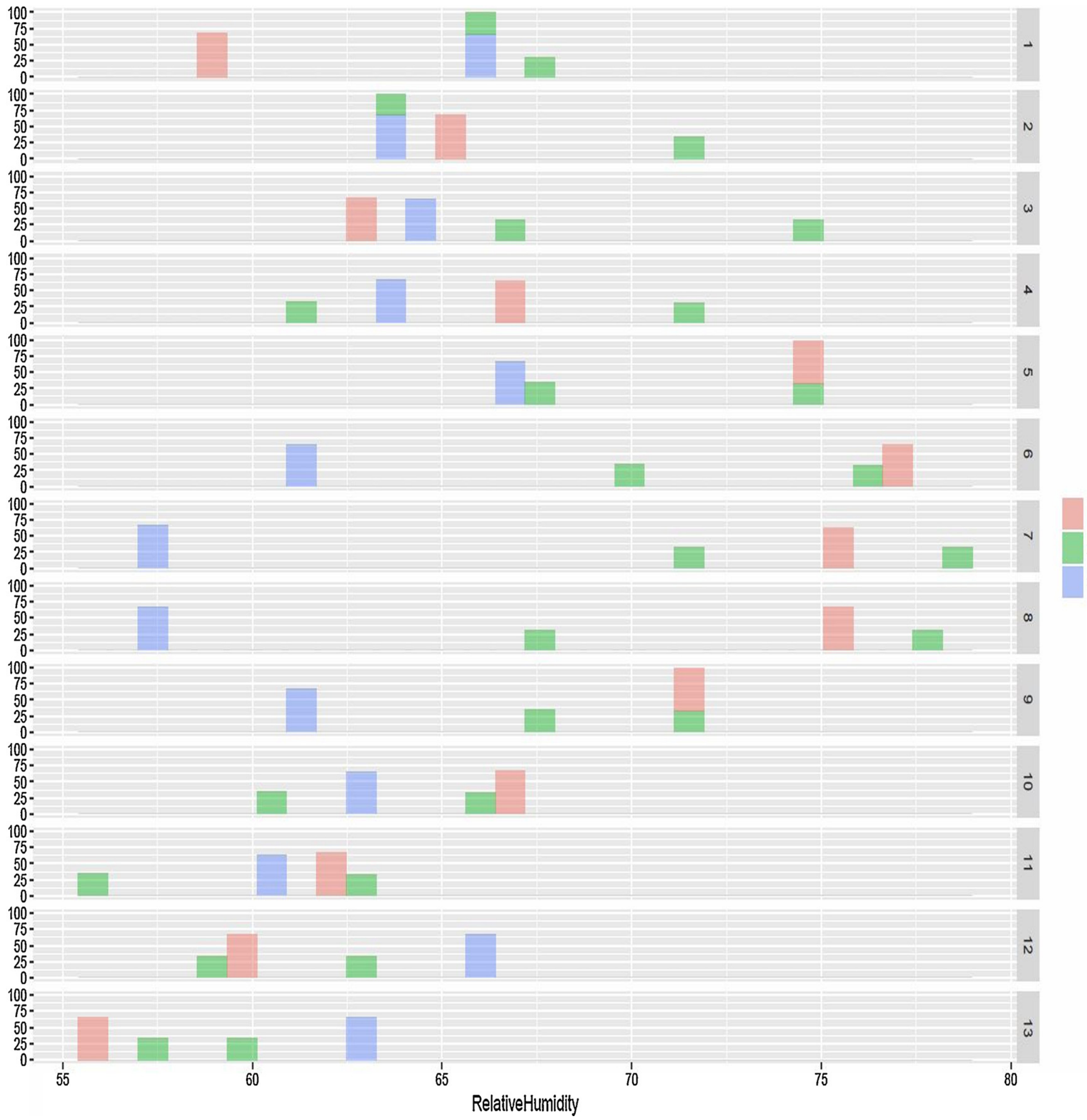

Fig. 2. Plot of "RelativeHumidity" (mean relative humidity) measured before and during every visit by farm. Farm 1 and 3 had one barn, farm 2 had two barns. Visit 1: end of July 2016; visit 7: mid-January 2017, visit 13: end of June 2017. Red: farm 1; green: farm 2; blue: farm 3 (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

39.42% showed a painful pododermatitis score at least once during data collection. In 30.15% of these cases, the pododermatitis score from the middle position had an intermittent progression alternating between painful scores (scores 4–6) and non-painful scores (scores 0–3).

Overall, we could observe 120 complete courses of development and recovery of painful pododermatitis in 95 does. A course was only complete if the doe started off with a non-painful score that developed into a painful score which either recovered to a non-painful score again, or if the animal died or was culled when it had a painful score during its last palpation. Due to the intermittent progression of pododermatitis, multiple observations per animal were possible. From these 120 occurrences of development and recovery of painful scores, 60.00%, 14.17% and 3.33% healed within 4, 8 or > 12 weeks, respectively, whereas 22.50% of the does died or were culled with a painful score. During the one-year period of data collection, a total of 144 does died (birth problems, pasteurellosis and emaciation, although mostly due to unknown causes) or were culled (mainly due to old age, emaciation, low fertility, severe pododermatitis and other diseases) and had to be replaced. Out of these 144 does, 10.42% had a score 4 and 8.33% had a score 5 when they were scored for the last time. The other 81.25% showed non-painful scores at the last palpation. The pododermatitis scores did not differ between does that remained in the study until the last palpation, and the does that were culled or died during the study on their last visit. However, there was a an interaction between culling/dying and age for pododermatitis scores (culling: $F_{1,338}$ = 1.29, NS, age: $F_{1,338}$ = 4.51, P = 0.03, interaction: $F_{1,338}$ = 3.73, P = 0.05). Culled or dying does were not older on average ($F_{1,342}$ = 2.36, NS) than the does that remained in the study.

4. Discussion

In this longitudinal study the same 201 adult female breeding rabbits were scored for pododermatitis every 4 weeks during one year on three commercial rabbit farms. Additionally, various potential risk factors for pododermatitis were recorded during every visit and analysed with an ABN modelling approach. Recently, this methodology has been applied to veterinary epidemiology (Ågren et al., 2017; McCormick et al., 2017; Pittavino et al., 2017; Wolff et al., 2017) mainly due to its ability to perform generalized standard regression.

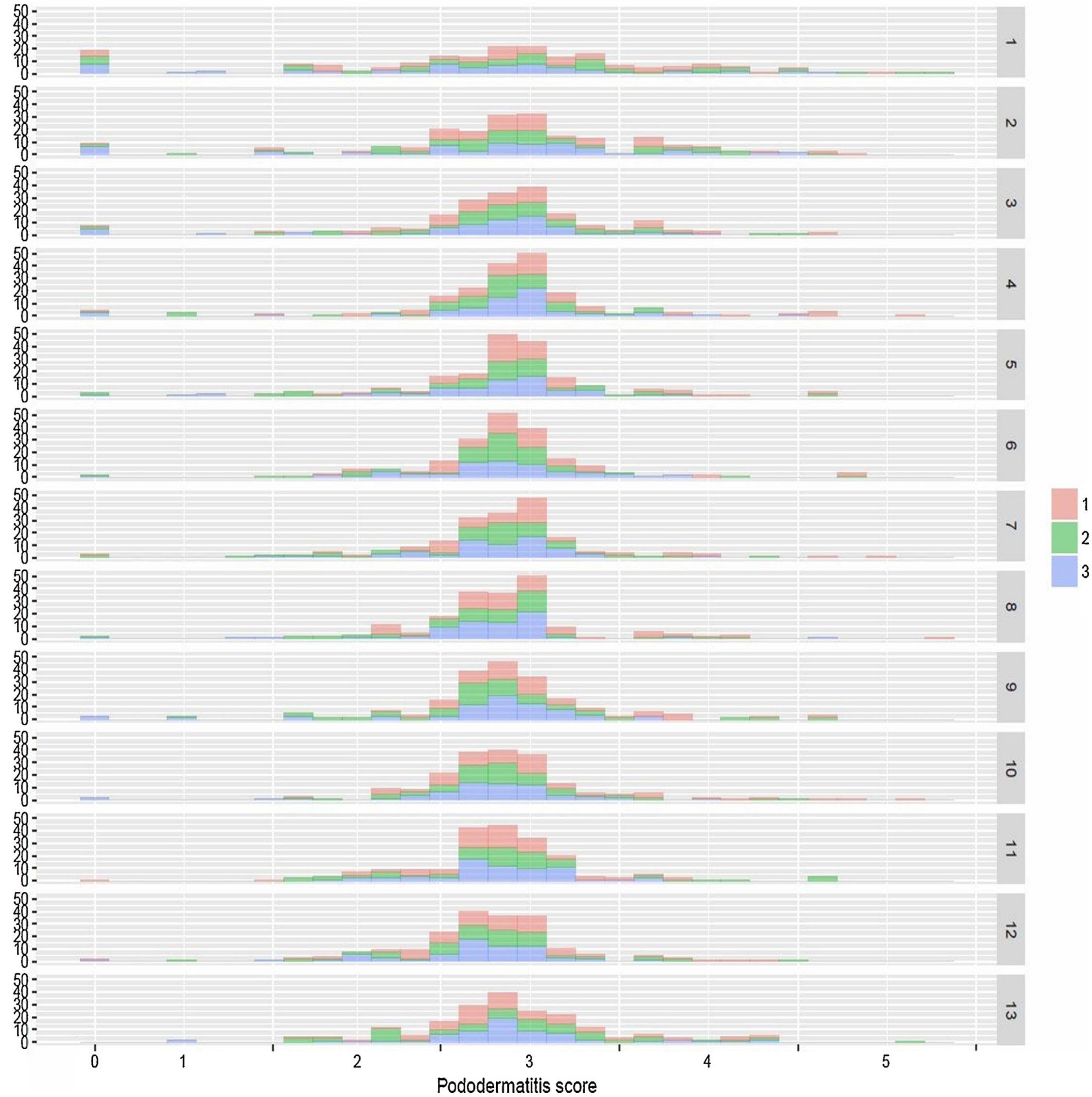

Fig. 3. Distribution of "PDmiddle" (mean of the two pododermatitis scores from the middle positions per animal) during every visit by farm. Red: farm 1; green: farm 2; blue: farm 3 (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

4.1. Risk factors

Confirming previous studies (EFSA, 2005; Olivas et al., 2013; Rommers and Meijerhof, 1996; Ruchti et al., 2018), claw length, body weight, age and number of kindlings were directly or indirectly associated with the pododermatitis score and thus were likely risk factors. As expected, claw length, body weight and number of kindlings were positively correlated with the age of the doe (Fig. 1 and Table 2). This means that the rabbits whose claws were classified as too long were 5.1 months older on average than animals with normal claw

Table 3
Transition matrix of the mean of the two pododermatitis scores from the middle positions of the hind legs per animal. The current score is arranged column-wise, the score at the next visit row-wise. The matrix is normalized by column which means that the numbers within are the probabilities to go from the current score to the row-wise score.

To	From											
	Score 0		Score 1		Score 2		Score 3		Score 4		Score 5	
	n	%	n	%	n	%	n	%	n	%	n	%
Score 0	17	30.4	2	10.0	11	3.2	1	0.1	0	0.0	0	0.0
Score 1	4	7.1	1	5.0	10	3.0	4	0.2	0	0.0	0	0.0
Score 2	22	39.3	7	35.0	103	30.5	178	10.9	8	4.5	0	0.0
Score 3	12	21.4	10	50.0	200	59.2	1329	81.4	117	65.4	11	35.0
Score 4	1	1.8	0	0.0	14	4.1	102	6.3	45	25.1	12	39.0
Score 5	0	0.0	0	0.0	0	0.0	18	1.1	9	5.0	8	26.0
Total	56	100	20	100	338	100	1632	100	179	100	31	100

length (Table 2). The claw length and farm were confounded, because the farmer of farm 3 cut the claws of the rabbits if they were too long. As only few does were replaced during each visit the mean age and the mean number of kindlings increased with each visit.

Pododermatitis was positively associated with relative humidity inside the barn. The relative humidity inside the barn of farm 3 differed from the values that were measured on farms 1 and 2, especially during wintertime (visit number 6 in December to visit number 9 in March). This difference can be explained by the location of the farms, as farm 3 was located at the top of a hill above the fog boundary and farms 1 and 2 were often shrouded in mist during wintertime. Naturally, the relative humidity itself was strongly negatively correlated with temperature. The relative humidity inside the barns was further positively associated with the moisture of the right hind leg.

As moist or wet fur on the hind legs was positively associated with relative humidity inside the barn, which in turn was positively correlated with the pododermatitis score, wet litter could have likely led to more severe pododermatitis. This is in agreement with other studies showing that hygiene (De Jong et al., 2008; Lebas et al., 1986 in Rommers and Meijerhof, 1996; Wolf and Speer, 2017) and the climate inside the barn (De Jong et al., 2008; Lebas et al., 1986 in Rommers and Meijerhof, 1996; Rosell et al., 2000 in Rosell and De la Fuente, 2009) influenced pododermatitis. Surprisingly our measure of wet litter, which represented the average wet area per pen (percent of the available area that was wet) that was corrected for the time of the last litter change, did not show any relationship with pododermatitis. Unfortunately, there were multiple problems why the moisture of the litter that the does encountered could not be assessed precisely. The wet area per pen could only be assessed in some pens per farm for time reasons and thus the values had to be averaged on farm level. Furthermore, we had no values of the wet area in the pens where the does stayed while they were non-pregnant, which usually seemed to be wetter compared to the pens with reproducing rabbits. As a follow-up it would be good to determine the influence of different moisture levels of the litter on the occurrence of pododermatitis experimentally.

In contrast to our expectations, the cleanliness of the left hind leg was negatively correlated with pododermatitis. This means that the pododermatitis score of a doe decreased when the fur of the paw changed from a clean to a dirty state. The respective arc in the DAG, however, is quite thin, which indicates that this was a very small effect although it was confirmed in the general linear model.

Overall, the distribution of the pododermatitis score from the middle position was quite narrow as 71.57% of the observations had a score of 3. This made it more difficult to detect correlations, especially if they were weak.

4.2. Development of pododermatitis over time

During the first visit, the prevalences of the pododermatitis scores were comparable to the results of the preceding cross-sectional study (Ruchti et al., 2018). Afterwards, the prevalence of score 3 increased, whereas the prevalences of the other scores slightly decreased (Fig. 3). As the nulli- and primiparous does in our study had lower scores compared to the prevalences of the scores of all observations, this shift could be due to the increase in the mean age of the does during data collection. The first and last visit were conducted in the same season (roughly within the same month) so a seasonal effect appears unlikely. Together with the transition matrix (Table 3) the data indicate a rather quick increase of the severity of pododermatitis to a score 3 in young does within a few months. Afterwards, most of them stayed at a score 3. The paws that developed into to a higher and presumably painful score most likely healed to a score 3 again within 4–8 weeks.

Compared to other studies (Buijs et al., 2014; De Jong et al., 2008; Mikó et al., 2012; Rommers and De Jong, 2009) that started with nulliparous does that had nearly healthy paws (mainly score 0, few with score 1), the nulli- and primiparous does in our study already showed pododermatitis. Therefore, we should also consider the housing conditions during the rearing period in future research projects on pododermatitis.

In contrast to many other studies (De Jong et al., 2008; EFSA, 2005; Rommers and De Jong, 2009; Sánchez et al., 2012; Szendrö and McNitt, 2012) that examined does housed on wire floors with or without plastic slats and who reported a progressive worsening of pododermatitis, we found that presumably painful scores often healed to non-painful scores in the Swiss group housing system. The healing in this study occurred without any treatment of the does. The only report of healing of sore hocks (wounds with exudates, ulcers or necrosis) were Rosell and De la Fuente, (2009) when they installed a plastic footrest on top of the wire floor.

Scoring lesions by palpation involves some error variance. Some healing events might be attributable to different assessments of identical states in subsequent visits. Overall, score 1 was difficult to detect (some score 1 might have been misclassified as score 0). The same might have happened with score 4 (some lesions of score 4 might have been misclassified as score 3) although this score was easier to detect than score 1. A limitation of this study is that it was not possible to measure the intra- or inter-observer reliabilities over time. Intra-observer reliability was only measured at the beginning of the cross-sectional study (Ruchti et al., 2018). Pictures of pododermatitis lesions could not be used, as it was impossible to take pictures of good quality, especially of small or multifocal lesions, and because the scores 1 and 2 would have been indiscernible as the hyperkeratosis can only be detected by palpation. As we assumed that the skin tissue cannot be preserved in a way that it looks (e.g. no loss of scabs and/or scales) and feels the same as in a living animal, we did not kill any does to keep their hind paws as a reference.

Severe pododermatitis was only one reason for culling a doe next to old age, emaciation, low fertility or other diseases thus it could not be quantified how often pododermatitis was the reason for culling. Since the score of pododermatitis was not higher in culled does than in does remaining in the experiment, pododermatitis did not seem to be an important factor for culling.

5. Conclusion

The body weight, number of kindlings, age and claw length of the does were positively associated with pododermatitis as the most important risk factors next to the relative humidity inside the barns (positive association) and the cleanliness of the plantar surface of the paws (weak negative correlation). To further investigate the causation between the moisture of the litter and the occurrence of pododermatitis, the litter moisture should be experimentally manipulated. The data of this longitudinal study indicate that the pododermatitis scores of young group housed breeding does in Switzerland increased from an inconspicuous score to a score 3 representing a hairless spot with thickened skin and scales on top of it within a few months. Afterwards, most of them stayed at this score whereas some does eventually proceeded to the presumably painful scores 4 and 5. It was shown that most of these painful scores healed to a non-painful score 3 within 4–8 weeks.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.prevetmed.2019.01.013.

References

Ågren, E.C.C., Frössling, J., Wahlström, H., Emanuelson, U., Sternberg Lewerin, S., 2017. A questionnaire study of associations between potential risk factors and salmonella status in Swedish dairy herds. Prev. Vet. Med. 143, 21–29. https://doi.org/10.1016/j.prevetmed.2017.05.004.

Andrist, C.A., van den Borne, B.H.P., Bigler, L.M., Buchwalder, T., Roth, B.A., 2013. Epidemiologic survey in Swiss group-housed breeding rabbits: extent of lesions and potential risk factors. Prev. Vet. Med. 108, 218–224. https://doi.org/10.1016/j.prevetmed.2012.07.015.

Buijs, S., Hermans, K., Maertens, L., Van Caelenberg, A., Tuyttens, F.A.M., 2014. Effects of semi-group housing and floor type on pododermatitis, spinal deformation and bone quality in rabbit does. Anim. Int. J. Anim. Biosci. 8, 1728–1734. https://doi.org/10.1017/S1751731114001669.

De Jong, I.C., Reimert, H., Rommers, J., 2008. Effect of floor type on footpad injuries in does: a pilot study. Ethol. Welf. 1171–1176.

Drescher, B., Schlender-Böbbis, I., 1996. Pododermatitis beim Kaninchen. Kleintierpraxis 41, 99–104.

EFSA, 2005. The Impact of the Current Housing and Husbandry Systems on Health and Welfare of Farmed Domestic Rabbits. pp. 1–31.

Harcourt-Brown, F., 2002. Chapter 9 - skin diseases. Textbook of Rabbit Medicine. Butterworth-Heinemann, Burlington, pp. 224–248. https://doi.org/10.1016/B978-075064002-2.50012-6.

Hess, L., Tater, K., 2012. Chapter 18: dermatologic diseases. Ferrets, Rabbits, and Rodents: Clinical Medicine and Surgery, third edition). Elsevier, pp. 232–244. https://doi.org/10.1016/B978-1-4160-6621-7.00018-X.

Kratzer, G., Furrer, R., 2018. Information-Theoretic Scoring Rules to Learn Additive Bayesian Network Applied to Epidemiology. ArXiv180801126 Cs Stat. .

Kratzer, G., Pittavino, M., Lewis, F., Furrer, R., 2017. abn: An R Package for Modelling Multivariate Data Using Additive Bayesian Networks.

Lewis, F.I., Ward, M.P., 2013. Improving epidemiologic data analyses through multivariate regression modelling. Emerg. Themes Epidemiol. 10, 4. https://doi.org/10.1186/1742-7622-10-4.

McCormick, B.J.J., Van Breda, L.K., Ward, M.P., 2017. Bayesian Network analysis of piglet scours. Sci. Rep. 7. https://doi.org/10.1038/s41598-017-06399-2.

Mikó, A., Szendrö, Z., Gerencsér, Z., Radnai, I., Odermatt, M., Nagy, I., Matics, Z., 2012. Performance of rabbit does in cages with or without elevated platform or plastic footrest. Proc. 10th World Rabbit Congr. Sharm El-Sheikh. pp. 441–445.

Mugnai, C., Bosco, A.D., Castellini, C., 2009. Effect of different rearing systems and pre-kindling handling on behaviour and performance of rabbit does. Appl. Anim. Behav. Sci. 118, 91–100. https://doi.org/10.1016/j.applanim.2009.02.007.

Olivas, I., Torres, A.G., Villagrá, A., 2013. Development of a pododermatitis score in breeding does using clustering methods. Anim. Int. J. Anim. Biosci. 7, 1011–1016. https://doi.org/10.1017/S1751731112002509.

Pittavino, M., Dreyfus, A., Heuer, C., Benschop, J., Wilson, P., Collins-Emerson, J., Torgerson, P.R., Furrer, R., 2017. Comparison between generalized linear modelling and additive Bayesian network; identification of factors associated with the incidence of antibodies against Leptospira interrogans sv Pomona in meat workers in New Zealand. Acta Trop. 173, 191–199. https://doi.org/10.1016/j.actatropica.2017.04.034.

R Development Core Team, 2016. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria.

Rommers, J.M., De Jong, I.C., 2009. Three mm wire floors with plastic mats prevent footpad injuries in rabbit does. Tagungsband 16 Int. Tag. Über Haltung Krankh. Kaninchen Pelztiere Heimtiere. pp. 113–119.

Rommers, J.M., Meijerhof, R., 1996. The effect of different floor types on footpad injuries of rabbit does. Proc. 6th World Rabbit Congr. Toulouse Vol2. pp. 431–436.

Rosell, J., De la Fuente, L., 2009. Effect of footrests on the incidence of ulcerative pododermatitis in domestic rabbit does. Anim. Welf. 18, 199–204.

Rosell, J.M., Dronda, M.A., De la Fuente, L.F., 2000. Enfermedades del Conejo. Mundi Prensa Libros SA, Madrid, Spain.

Ruchti, S., Meier, A.R., Würbel, H., Kratzer, G., Gebhardt-Henrich, S.G., Hartnack, S., 2018. Pododermatitis in group housed rabbit does in Switzerland—prevalence, severity and risk factors. Prev. Vet. Med. 158, 114–121. https://doi.org/10.1016/j.prevetmed.2018.06.011.

Sánchez, J.P., de, la F., Rosell, J.M., 2012. Health and body condition of lactating females on rabbit farms. J. Anim. Sci. 90, 2353–2361. https://doi.org/10.2527/jas.2011-4065.

Seaman, S.C., Waran, N.K., Mason, G., D'Eath, R.B., 2008. Animal economics: assessing the motivation of female laboratory rabbits to reach a platform. Anim. Behav. 75, 31–42.

Szendrö, Z., McNitt, J.I., 2012. Housing of rabbit does: group and individual systems: a review. Livest. Sci. 150, 1–10. https://doi.org/10.1016/j.livsci.2012.09.017.

Wolf, P., Speer, R., 2017. Einflüsse verschiedener einstreumaterialien auf die Fussballengesundheit bei Kaninchen in der Heimtierhaltung. 20. Internationale Tagung Über Haltung Und Krankheiten Der Kaninchen, Pelztiere Und Heimtiere 62–71.

Wolff, C., Boqvist, S., Ståhl, K., Masembe, C., Sternberg-Lewerin, S., 2017. Biosecurity aspects of cattle production in Western Uganda, and associations with seroprevalence of brucellosis, salmonellosis and bovine viral diarrhoea. BMC Vet. Res. 13, 382. https://doi.org/10.1186/s12917-017-1306-y.

Web references

https://www.kontrolldienst-sts.ch/html/index.php/de/coop-bts-kaninchen, accessed 23/10/2017

http://www.eurolap.fr/en/hylamax.html, accessed 10/04/2018

http://www.eurolap.fr/en/hyla-ng.html, accessed 10/04/2018

http://www.hycole.com/en/, accessed 23/10/2017

http://www.zika-kaninchen.de/, accessed 23/10/2017

www.schweizerkaninchen.ch, accessed 16/10/2017